

IN THE CLAIMS

1. (previously presented) A method for biotechnologically producing valuable products in which a medium is fed from an upstream feed receptacle (2, 3, 4) to a bioreactor (1) by a feed line (7, 9, 11) and subjected to a fermentation process and in which the valuable product is harvested, as filtered permeate in a first downstream harvest receptacle (16) and/or as concentrated retentate in a second harvest receptacle (18), by way of a single downstream cross-flow filtration unit (5) connected to said bioreactor (1) by a conveying line (13) and a retentate line (17), and connected to said first downstream harvest receptacle (16) by a permeate line (15), and residues are supplied again to the bioreactor until harvesting as retentate by said retentate line (17), wherein said retentate can be removed from the bioreactor by a harvest line (19) connected to said second harvest receptacle (18) for storing a cell-contaminated harvest of the retentate, said method further characterized in that, in addition to the medium, other substances can be fed to the bioreactor (1) in a controlled manner, in that the concentrated retentate and the permeate can be harvested in a controlled manner and in that the fermentation process and the filtration are regulated, in a manner in which they are matched to each other in an integrated system, by way of a control unit (6).

2. (original) The method as claimed in claim 1, characterized in that the integrated system can be cleaned and sterilized in situ, with this being controlled by the control unit (6).

3. (previously presented) The method as claimed in claim 1, characterized in that recombinant proteins are produced as valuable products, with the permeate yielding a cell-free harvest and the retentate yielding a cell-contaminated harvest.

4. (previously presented) The method as claimed in claim 1, characterized in that the method proceeds while being conducted in a sequential and integrated manner.

5. (previously presented) The method as claimed in claim 3, characterized in that, in a batch phase (29), cells which are supplied to the bioreactor (1) adapt to the medium and,

in a subsequent fed batch phase (30), the cells are propagated at a constant growth rate by means of feeding.

6. (previously presented) The method as claimed in claim 3 characterized in that, in a production phase (31), the induction of product formation, and the actual production of the recombinant proteins, take place by means of adding an inducing substance.

7. (original) The method as claimed in claim 6, characterized in that the concentration of the inducing substance is measured by way of flow diffusion analysis and regulated by feeding from a second feed receptacle (3).

8. (previously presented) The method as claimed in claim 4, characterized in that, in a product harvesting phase (32), a part of the bioreactor (1) is harvested cell-free.

9. (original) The method as claimed in claim 8, characterized in that, in a cell harvesting phase (33), cell mass in the retentate is harvested and this is followed by a medium refreshing phase (34) involving the feeding of medium (35).

10. (original) The method as claimed in claim 9, characterized in that, after the medium refreshing phase (34), the cyclic process, in which, except in the product harvest, only the retentate stream, and not the permeate stream, is to flow, begins once again with the production phase (31).

11. (previously presented) The method as claimed in claim 3, characterized in that the recombinant proteins are produced using the yeast *Pichia pastoris*.

12. (original) The method as claimed in claim 11, characterized in that methanol (36) is added, as inducing substance, to the medium (35) in the bioreactor (1) in order to induce the sequences of the cell protein.

13. (original) The method as claimed in claim 12, characterized in that the methanol concentration is maintained at a constant level.

14. (previously presented) The method as claimed in claim 11, characterized in that glycerol (37) is fed in, in the fed batch phase (30) and/or in the production phase (31), for increasing production.

15. (previously presented) The method as claimed in claim 1, characterized in that the method proceeds while being conducted in a continuous and integrated manner.

16. (original) The method as claimed in claim 15, characterized in that the production phase (31), the product harvesting phase (32) and the cell harvesting phase (33) proceed in parallel.

17. (previously presented) A device for biotechnologically producing valuable products, comprising a bioreactor (1) having an upstream first feed receptacle (2) for a medium and a single downstream cross-flow filtration unit (5) whose permeate line (15) is connected to a first harvest receptacle (16) and whose retentate line (17) leads back into the bioreactor (1), characterized in that at least one second feed receptacle (3) containing an inducing substance is located upstream of the bioreactor (1), in that a second harvest receptacle (18) for a cell-contaminated harvest of the retentate is connected to the bioreactor (1) by way of a harvest line (19), and in that a control unit (6) is arranged for measuring and regulating the fermentation and filtration process.

18. (original) The device as claimed in claim 17, characterized in that, for the purpose of measuring the concentration of the inducing substance in the bioreactor (1), the control unit (6) possesses an analytical system (24) which measures the concentration of the inducing substance by way of a sensor which is arranged in the bioreactor (1) and regulates the concentration of inducing substance in the bioreactor (1) by controlling a second feed pump (9) which is located upstream of the second feed receptacle (3).

19. (original) The device as claimed in claim 18, characterized in that the analytical system (24) is in the form of a flow diffusion analysis (FDA) system.

20. (previously presented) The device as claimed in claim 17, characterized in that, for the purpose of measuring a cell concentration in the bioreactor (1), the control unit (6) possesses a second analytical system (27) which measures the cell concentration by way of a second sensor (28) which is arranged in the bioreactor (1) and regulates the cell concentration in the bioreactor (1) by controlling a harvest pump (20) which is located upstream of the second harvest receptacle (18).

21. (previously presented) The device as claimed in claim 17, characterized in that, for the purpose of regulating the addition of medium to the bioreactor (1), a third regulator (44) is connected to a feed pump (8) by way of a weighing device (22) belonging to the bioreactor (1).